

**AWARD NUMBER: W81XWH-14-1-0236**

**TITLE:** "Hippocampal and Cognitive Function, Exercise, and Ovarian Cancer: A Pilot Study"

**PRINCIPAL INVESTIGATOR:** Richard Sloan, PhD

**CONTRACTING ORGANIZATION:** Columbia University  
New York, NY 10032-3702

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Fort Detrick, Maryland 21702-5012

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# REPORT DOCUMENTATION PAGE

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<b>13. SUPPLEMENTARY NOTES</b> n/a						
<b>14. ABSTRACT</b> In this application, we propose to address this problem by focusing primarily on a single post-chemotherapy complaint in a single cancer: problems with memory in patients with ovarian cancer. We focus on this problem for three reasons: 1) according to the Ovarian Cancer National Alliance, memory problems are among the most frequently cited by patients; 2) by narrowly targeting our inquiry, we will avoid the "noise" in the data associated with different treatment regimens and correspondingly different cognitive complaints and; 3) there are decades of neuroscience research, some of it from our group, indicating that memory impairment, such as the kind reported in the context of chemotherapy, is mediated primarily by a region of the brain called the hippocampus. In this application, we propose to investigate the possibility that standard chemotherapy regimen used to treat ovarian cancer leads to memory impairment because it arrests the normal processes of neurogenesis, the growth of new nerve cells, in this brain region. In addition, because a growing body of research studies shows that physical exercise leads to improvement in memory and learning and that exercise targets the same brain regions responsible for chemotherapy-induced memory problems, we propose to conduct a pilot study of an intervention to increase patients' physical activity to test whether this will slow this effect of chemotherapy on nerve cell growth in the hippocampus and subsequently offset memory decline.						
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**“Hippocampal and Cognitive Function, Exercise, and Ovarian Cancer: A Pilot Study”**

**Proposal Log Number OC130386,  
Award Number W81XWH-14-1-0236  
HRPO Log Number A-18125  
Reporting Period: 8/1/14 – 7/31/15**

**1 INTRODUCTION:**

*In this application, we propose to address this problem by focusing primarily on a single post-chemotherapy complaint in a single cancer: problems with memory in patients with ovarian cancer. We focus on this problem for three reasons: 1) according to the Ovarian Cancer National Alliance, memory problems are among the most frequently cited by patients; 2) by narrowly targeting our inquiry, we will avoid the “noise” in the data associated with different treatment regimens and correspondingly different cognitive complaints and; 3) there are decades of neuroscience research, some of it from our group, indicating that memory impairment, such as the kind reported in the context of chemotherapy, is mediated primarily by a region of the brain called the hippocampus. In this application, we propose to investigate the possibility that standard chemotherapy regimen used to treat ovarian cancer leads to memory impairment because it arrests the normal processes of neurogenesis, the growth of new nerve cells, in this brain region. In addition, because a growing body of research studies shows that physical exercise leads to improvement in memory and learning and that exercise targets the same brain regions responsible for chemotherapy-induced memory problems, we propose to conduct a pilot study of an intervention to increase patients’ physical activity to test whether this will slow this effect of chemotherapy on nerve cell growth in the hippocampus and subsequently offset memory decline.*

**2 KEYWORDS:**

*Physical activity interventions, ovarian cancer treatment, chemotherapy-induced cognitive dysfunction*

**3 ACCOMPLISHMENTS:**

**Major Goals/Objectives:**

- 1.Approval by CUMC Herbert Irving Comprehensive Cancer Center (HICCC) Protocol Review and Monitoring Committee  
Date of Completion: 4/17/14 (100% completed)
- 1A. Approval of HICCC protocol materials by DoD HRPO; Respond to DoD HRPO questions  
100% completed
- 2.Approval by New York State Psychiatric Institute (NYSPI) Institutional Review Board  
Date of Completion: 5/15/15 (100% completed)
- 2A. Approval of NYSPI IRB materials by DoD HRPO; Respond to DoD HRPO questions  
Date of Completion: June 1, 2015 (100% completed)
- 3.Training research assistant “coach” in patient recruitment, retention, delivery of walking intervention  
Date of Completion: July 1, 2015 (100% completed)
- 4.Training research assistant in administration and scoring of neuropsychology tests  
Date of Completion: July 1, 2015 (100% completed)
- 5.Training research assistant in image analysis  
Date of Completion: July 1, 2015 (100% completed)
- 6.Recruiting 21 ovarian cancer patients 4-6 weeks post-surgery  
August 1, 2016: 5% completed
- 7.Pre- and post-intervention neuropsychology and imaging data collection and scoring  
August 1, 2016: 5% completed
- 8.Delivering the interventions to the two treatment groups

August 1, 2016: 5% completed

#### 9.Data analysis

August 1, 2016: 5% completed

#### 10.Post-Analysis: Submission of findings to national meetings, proposal to DoD or NIH for definitive study (if appropriate)

August 1, 2016: 0% completed

#### **What was accomplished under these goals?**

*This is a study to assess the feasibility of recruiting ovarian cancer patients in a pilot study to assess the impact of increasing physical activity on neuropsychological and brain imaging outcomes. The principle finding to date is that due to changing treatment protocols, it is extremely difficult to recruit patients into the study. To date, we have screened 739 post-operative patients and have recruited only 1. With the exception of 4 patients, all others failed to meet inclusion/exclusion criteria. Of the 4 who met criteria, only one agreed to participate.*

#### **What opportunities for training and professional development has the project provided?**

*Nothing to report*

#### **How were the results disseminated to communities of interest?**

*Nothing to report*

#### **What do you plan to do during the next reporting period to accomplish the goals?**

*We have expanded our potential pool of patients to those with endometrial and uterine cancers in the hope that we will be able to recruit more patients.*

### **IMPACT:**

#### **What was the impact on the development of the principal discipline(s) of the project?**

*Nothing to report*

#### **What was the impact on other disciplines?**

*Nothing to report*

#### **What was the impact on technology transfer?**

*Nothing to report*

#### **What was the impact on society beyond science and technology?**

*Nothing to report*

### **CHANGES/PROBLEMS:**

#### **Changes in approach and reasons for change**

*To increase recruitment, we have opened enrollment to endometrial and uterine cancer patients.*

#### **Actual or anticipated problems or delays and actions or plans to resolve them**

*As this is a feasibility study, we have encountered significant problems with recruitment, due in large part to changes in treatment protocols.*

#### **Changes that had a significant impact on expenditures**

*Nothing to report*

#### **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

*IRB approval to recruit endometrial and uterine cancer patients: January 16, 2016*

*IRB approval to recruit patients receiving both chemotherapy and radiotherapy: May 27, 2016*

#### **Significant changes in use or care of human subjects**

*IRB approval to recruit endometrial and uterine cancer patients: January 16, 2016*

*IRB approval to recruit patients receiving both chemotherapy and radiotherapy: May 27, 2016*

**Significant changes in use or care of vertebrate animals.***Nothing to report***Significant changes in use of biohazards and/or select agents***Nothing to report***PRODUCTS:****Publications, conference papers, and presentations:****Journal publications.***Nothing to report***Books or other non-periodical, one-time publications.***Nothing to report***Other publications, conference papers, and presentations.***Nothing to report***Website(s) or other Internet site(s)***Nothing to report***Technologies or techniques***Nothing to report***Inventions, patent applications, and/or licenses***Nothing to report***Other Products***Nothing to report***PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:****What individuals have worked on the project?**

<b>Name:</b>	<i>Richard Sloan, PhD</i>
<b>Project Role:</b>	<i>Principal Investigator</i>
<b>Researcher Identifier (e.g. ORCID ID):</b>	<i>n/a</i>
<b>Nearest person month worked:</b>	<i>1</i>
<b>Contribution to Project:</b>	<i>Dr. Sloan is responsible for all aspects of the study including recruitment of patients, oversight of the activity-increasing program, and data analysis.</i>
<b>Funding Support:</b>	<i>Columbia University internal funds</i>
<b>Name:</b>	<i>Scott Small, MD</i>
<b>Project Role:</b>	<i>Co-Investigator</i>
<b>Researcher Identifier (e.g. ORCID ID):</b>	<i>n/a</i>
<b>Nearest person month worked:</b>	<i>1</i>
<b>Contribution to Project:</b>	<i>Dr. Small supervises all aspects of the imaging within the proposed project and supervises the half-time Research Assistant in scoring the imaging data.</i>
<b>Funding Support:</b>	<i>Columbia University internal funds</i>
<b>Name:</b>	<i>Adam Brickman, PhD</i>
<b>Project Role:</b>	<i>Co-Investigator</i>
<b>Researcher Identifier (e.g. ORCID ID):</b>	<i>n/a</i>

<i>Nearest person month worked:</i>	1
<i>Contribution to Project:</i>	<i>Dr. Brickman will oversee the neuropsychological evaluation of participants in the study, including training study personnel on task administration, scoring, quality assurance, and data entry.</i>
<i>Funding Support:</i>	<i>Columbia University internal funds</i>
<b>Name:</b>	<b><i>Jason Wright, MD</i></b>
<i>Project Role:</i>	<i>Co-Investigator</i>
<i>Researcher Identifier (e.g. ORCID ID):</i>	<i>n/a</i>
<i>Nearest person month worked:</i>	1
<i>Contribution to Project:</i>	<i>Dr. Wright will be responsible for patient recruitment as well as medical oversight for patients recruited to the study.</i>
<i>Funding Support:</i>	<i>Columbia University internal funds</i>
<b>Name:</b>	<b><i>Jose Henriquez-Rivera</i></b>
<i>Project Role:</i>	<i>Technician B</i>
<i>Researcher Identifier (e.g. ORCID ID):</i>	<i>n/a</i>
<i>Nearest person month worked:</i>	1
<i>Contribution to Project:</i>	<i>Mr. Henriquez-Rivera is the study “coach” and his responsibilities include patient recruitment, retention, delivery of walking intervention.</i>
<i>Funding Support:</i>	

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

*Nothing to report*

**What other organizations were involved as partners?**

*Nothing to report*

#### **SPECIAL REPORTING REQUIREMENTS:**

*n/a*

#### **APPENDICES:**

*n/a*